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SCHOOL OF MEDICINE
OFFICE OF THE DEAN
TELEPHONE: (530) 752-0321
FAX: (530) 752-1532

ONE SHIELDS AVENUE
DAVIS, CALIFORNIA 95616

Michael Wilkes, M.D., Ph.D.
Professor of Medicine and
Vice Dean, Medical Education
SCHOOL OF MEDICINE

10 June 2006

Congressman Henry Waxman
Ranking Minority Member
Committee on Government Reform
U.S. House of Representatives
Washington, D.C. 20515

Dear Congressman Waxman:

At your request, I have carefully reviewed the material provided by the Food and Drug Administration to the Committee on Government Reform. My concerns with these materials relate to the enforcement of Section 505 of the Federal Food, Drug and Cosmetic Act. This Section of the Act prohibits the marketing of any drug without a new drug application. Further, Section 502 addresses issues related to drug labeling.

In Appendix "A" I have addressed my specific concerns based on the case files provided by your office. Please note that many of the files provided to me contained only partial documentation. Further, I understand that FDA did not provide data as to what percentage of field office recommendations these files represent. As a result, I can not fully assess the extent of the problems related to failure of the FDA to follow up on District Office concerns. However, collectively, the files I have reviewed paint a picture of a central administration at the FDA that has systematically ignored District Field Officers and regularly overridden their explicit and well documented concerns about drug safety and public health.

The concerns raised by the District Offices are often, although not always, significant concerns that could (and in all likelihood did) lead to patient harm. In some cases the harm may be physical or physiological, where the patient suffers direct adverse effects from using the product. In other cases, physical harm may result from a patient choosing not to visit a physician because of a belief that the medical problem is being addressed by the drug, when the drug in reality is ineffective. The harm in other cases may be economic, where consumers purchase expensive products that have no effect.

After the thalidomide disaster, legislators recognized that the drug approval process had to be more tightly controlled. In 1962 Congress expanded the FDA's powers by passing the Kefauver-Harris Drug Amendments Act, which required scientists to prove that a

drug was safe and effective before it could be sold to the American public. In many of the cases provided by FDA these Amendments seem to be substantially ignored both in fact and in spirit. In fact, many of the District Office observations and recommendations mentioned in Appendix "A" are identical to observations made in the early 20th Century about snake oil salesmen who went from town to town across America selling nostrums and potions that often contained dangerous compounds, often contained alcohol, and almost never contained anything proven to be effective. Today the snake oil salesmen need not travel in horse and cart nor even in automobiles – they use the internet and the mail to make the same outrageous claims with products that contain sometime dangerous ingredients and often inert, useless ingredients. And the Food and Drug Administration seems unable and unwilling to step in to protect the American public.

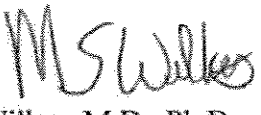
I am also alarmed at the large number of cases where CDER disapproved a warning letter because CDER itself had missed an internal deadline. It is disturbing that so many – in my opinion, way too many – CDER actions were issued over a year after the district's recommendation. In some cases the "letter of disapproval" contained only a few short paragraphs, yet CDER took 18-20 months to respond. Given the dangers – real and potential – this is unacceptable. Such delay would not be tolerated in academics or in business. Why should we accept this from the government agency charged with protecting our health?

My conclusion based on these files is that the FDA systematically ignores District Office recommendations. Given that these files involve District Offices all over the nation, I can only conclude that the District Offices are not all at fault, but rather that we have a non-responsive and anti-regulatory administration at the FDA.

My further concern is that the systematic "disapproval" of recommendations by CDER can only lead to low morale in the District Offices. After these impressive and thorough district investigations were dismissed on such unreasonable grounds, I can not imagine the field staff feeling anything other than discouraged and demoralized. This has the great potential to lead to an altered work effort. Field staff might approach future violations of the law more permissively, reasoning "why put in the effort to conduct a careful investigation if my recommendations will take a year to be acted upon and then, in all likelihood, will be rejected?"

I hope that this overview is of some assistance. Please let me know if I can be of further assistance.

Sincerely,



Michael Wilkes, M.D., Ph.D.
Professor of Medicine
Vice Dean, Medical Education
School of Medicine
University of California, Davis

Appendix A: SPECIFIC COMMENTS:

Manufacturer (product)	District Recommendation	FDA – CDER Response	Comments of Dr. Michael Wilkes
Vale Enterprises (Hangover Formula)	**Issue Warning Letter** **Reason:** Toxic levels of caffeine contained in product.	**Warning Letter Returned to District – not approved.** There was a significant delay in the FDA's response (actual dates not provided). CDER concluded that the high doses of caffeine do not make the product a drug rather than a food supplement. Further, CDER concluded that the concerns did not meet "the regulatory significance threshold for enforcement."	In this case there is a report of actual patient harm to three individuals. I am concerned that with at least three known illnesses caused by the ingestion of this drug CDER's threshold needs recalibration.
Tarmac Products (Neoasma Tablets)	**Issue a Warning Letter**	**Disapproved** due to CDER failing to act within the four-month deadline set by the Office of General Counsel for warning letter review. Further, the FDA wrote, "we are not prepared to support new drug and misbranded charges for cough and cold preparations."	For decades, cold and cough preparations have been major culprits in misbranding and containing dangerous chemicals. After the passage of the Food and Drug Act and the amendments this was to improve for new drugs. It is unclear why the FDA is taking no action on this class of drugs. It is also important to recognize that this product appears to contain theophylline which is well known to have significant and dangerous side effects. In the opinion of most expert groups theophylline is never a first or second line therapy. I teach that it has no place in asthma therapy. Further, I believe it is NEVER recommended to be used for children (counter to the recommendation in the following Tarmac website) This product continues to be available at a variety of websites, including: http://www.rxzone.us/product.cfm/rx/PRESCRIPTIONS-MEDICATIONS/Prescription-Medications---N/Neoasma-Tablets-48-449256.html and http://www.tarmacproducts.com/neoasma.html.

Manufacturer (product)	District Recommendation	FDA – CDER Response	Comments of Dr. Michael Wilkes
Answered Prayers (Helen Pensanti MD ProHELP Natural Progesterone Menopause Relief Cream; Phosphatidylserine Capsules Brain Food)	**Issue a Warning Letter** **Reason:** Marketing a product containing OTC hormones without FDA approval. The investigation resulted from a consumer's complaints about burning of the skin. The Brain Food product implies that the product is effective for treating multiple sclerosis (which is false). The district investigation determined multiple instances of outright deceit by firm officials.	**Warning Letter Disapproved** "Not enough evidence…."	There are many hormone containing products that Dr. Helen Pensanti produces seemingly without any interference from the FDA. She seems not to be board certified and it is unclear where she went to medical school (her bio on the website does not mention this although it does state that she did not finish residency. The products are available at: http://www.askdrhelen.com/about.html. Most of these products contain a well known hormone (progesterone) as an active ingredient. This hormone can have negative effects when used for inappropriate purposes. Further, the firm makes statements that natural hormones are safe and that the dangers of hormones arise only when they are synthetic. I know of no data that separates natural from synthetic hormones in terms of safety. Further, arsenic, carbon monoxide and cyanide are all natural – and clearly deadly. Natural does not equal safe!
(Topical creams: Aminophylline cream; glucosamine cream with emu oil; progesterone cream, prostate treatment cream; and other products)	**Issue a warning letter.** **Reason:** The products contain potent hormones (e.g., prenenolone, progesterone). Further, the promotional material states that the new drugs help the body adjust to cyclical changes without the side effects of prescription drugs. This is false.	**Do not issue due to "low priority."**	This seems to be an enormous error by CDER. Aminophylline and other chemicals contained in the products are dangerous and the field officers had a clear, well documented investigation. Aminophylline is a well known toxic chemical that is regulated by the FDA. It has a narrow toxic to therapeutic ratio, meaning that the range of dosages in which it is effective but not toxic is very small.
(Skin protectant; insect repellant; sunscreen; and body lotion)	**Issue a warning letter.** **Reason:** Marketing an unapproved new drug, failing to following proper marketing practices, and misbranding of products.	**Warning letter disapproved** It took 11 months for the FDA to act on the recommendation. The disapproval is based on a perception of "low risk."	These products would lead a reasonable consumer to assume that they offer protection from the sun which is not proven and seems unlikely. The delay seems an unacceptably long period of time when safety is at stake. I would place the concern at a moderate level.

Manufacturer (product)	District Recommendation	FDA – CDER Response	Comments of Dr. Michael Wilkes
(Dietary supplement)	**Issue Warning Letter** **Reason:** The product contains a chemical (porcine relaxin) that is not a dietary supplement. The product is not manufactured in compliance with manufacturing standards. The chemical involved is not recognized by experts to be effective or safe. There is no evidence that the product works as an anti-aging product as marketed. There is no evidence that the product works on fibromyalgia, as marketed.	**Placed in permanent Abeyance.** It took nearly 24 months for the FDA to act on the recommendation.	The delay seems unacceptably long when safety is at stake. I can find little data on procine relaxin so I can not assess its dangers. However, its effectiveness seems dubious.
(Over-the-counter drug to treat indigestion)	**Issue Warning Letter** **Reason:** Marketing unapproved drug and poor manufacturing practices including no or poor quality control. Firm was cited in 1999 for failure to correct all deficiencies.	**Warning letter disapproved seven months later.** The FDA felt that drug was considered "grandfathered in."	Dallas District Compliance Branch makes a strong argument that the manufacturer is claiming new indications, which would justify a warning letter.
(External analgesic and itch cream)	**Issue Warning Letter** **Reason:** Marketing unapproved drug, misbranding and poor manufacturing practices. No active ingredient found in the product.	**Warning Letter Disapproved** It took the FDA 11 months to respond to the district office's recommendation.	It is fraudulent to promote a drug as containing an active ingredient if, in fact, none is present. Further, CDER seems to excuse the absence of the ingredient by the mere fact that the manufacturer "is a very small operation." I see that as irrelevant.

Manufacturer (product)	District Recommendation	FDA – CDER Response	Comments of Dr. Michael Wilkes
(Body-building dietary supplement)	**Issue Warning Letter** **Reason**: Marketing a product that by its own marketing material contains a "potent thyroid hormone." The District Office suggests that the product presents a significant risk of illness or injury.	**Warning Letter Disapproved.** It took the FDA 18 months to respond to the district's recommendation.	This is a product with significant potential for abuse and the promotion of ill health. While it is unclear who is actually responsible (manufacturer, distributor, or retail seller) there is a likelihood of potential harm.
(Facial treatment astringent skin cleaner and refresher and other products)	**Issue Warning Letter** **Reason:** Improper labeling and failure to follow good manufacturing processes.	**Warning Letter Disapproved** It took the FDA 10 months to act on the recommendation. The warning letter was disapproved due to the "post inspection deadline having passed."	This is an embarrassment. They missed the internal deadline for taking action so the product remains on the market. This suggests significant management problems at the FDA.
(Homeopathic creams, ointments, and mouthwash)	**Issue a warning letter** **Reason:** The district office is concerned that the products contain over 50% ethyl alcohol and are offered for treatment of minor mouth irritations. Products also are recommended as inhalants for respiratory complaints and as treatment for alcohol overindulgence. This drug could cause problems for consumers, and particularly for those who are not allowed to consume products containing alcohol.	**Warning Letter Disapproved.** While CDER agreed that deficiencies existed, it only recommended that the district office "meet with the firm." It based this conclusion on the small size of the firm and the fact that the recommendation exceeded the four-month deadline set by the Office of General Counsel (OGC) for warning letter review.	This is outrageous. The FDA time and time again fails to meet the four-month deadline for review of warning letters. This appears to be either a conspiracy at FDA intended to systematically ignore the district office's concerns or gross incompetence. Marketing this type of snake oil was the exact reason The Food and Drug Act was originally passed. It is remarkable that this type of sale is still permitted.

Manufacturer (product)	District Recommendation	FDA – CDER Response	Comments of Dr. Michael Wilkes
(Injectable drugs)	**Issue Warning Letter** **Reason:** Genotropin in combination with injectable vitamins and lidocaine prior to laser therapy is an unapproved use of the medicines.	**Warning Letter Disapproved – untitled letter authorized.** It took the FDA over 23 months to respond to the district's recommendation.	Genotropin is an approved drug of human growth hormone. It is used in some children with growth retardation due to low levels of endogenous hormone production. Growth hormone has no proven value in adults and there are no studies that show that local injections relieve arthritic pain or other type of musculo-skeletal pain. There is evidence that the drug is costly and may be dangerous if absorbed systemically which is almost certainly is.
(Cough syrup)	**Issue Warning Letter** **Reason:** Failure to comply with good manufacturing standards; dangerous manufacturing practices.	**Warning Letter Disapproved**	It is encouraging that the company destroyed the product voluntarily. However, the issuance of a warning letter would have served as a formal warning to the firm should it decide to import this product again, laying the groundwork for future enforcement action.